

# Orbital Involvement in Cherubism: Computed Tomographic and Three-Dimensional Imaging Findings: Case Report

## Şerubizmde Orbital Tutulum: Bilgisayarlı Tomografi ve Üç Boyutlu Görüntüleme Bulguları

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**ABSTRACT** Cherubism is a rare hereditary benign lesion of the mandible that appears in childhood as bilateral painless swellings that progress until puberty, and then spontaneously regress. It was first described in 1933 and referred to as familial multilocular cystic disease of the mandible. These lesions are rarely seen and the diagnosis of the lesion requires the integration of the histopathology with history, clinical course of the disease and the radiographic appearance. Plain radiographs and computed tomography (CT) scan are sufficient for radiological diagnosis. Orbital involvement secondary to cherubism is rare. In this article, we describe CT and three-dimensional (3D) imaging features in two cases with extensive orbital involvement of cherubism.

**Key Words:** Jaw diseases; cherubism; tomography scanners, x-ray computed; imaging, three-dimensional

**ÖZET** Şerubizm, puberteye kadar ilerleyici, daha sonra kendiliğinden gerileyen iki taraflı ağrısız mandibular şişlik ile karakterize çocukluk çağı nadir herediter benign lezyonudur. İlk kez 1933 yılında mandibulanın ailesel multiloküler kistik hastalığı olarak tanımlanmıştır. Bu lezyonlar nadir görülür ve lezyonun tanısı radyografik görünüm, hastalık öyküsü ve klinik seyri ile histopatolojik bulgular temelinde yapılır. Direkt röntgenografiler ve bilgisayarlı tomografi (BT), radyolojik tanı için yeterlidir. Şerubizme sekonder orbital tutulum nadirdir. Bu yazıda, şerubizme bağlı yaygın orbital tutulumu olan iki olguda BT ve üç boyutlu (3B) görüntüleme özellikleri tanımlanmaktadır.

**Anahtar Kelimeler:** Çene hastalıkları; şerubizm; bilgisayarlı tomografi; üç boyutlu görüntüleme

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Cherubism is a very rare, hereditary, fibrous dysplasia of the jaws which usually produces massive bilateral enlargement of the maxilla and mandible. The renaissance cherubic appearance of the eyes, 'raised to heaven', appears due to enlargement of the lower half of the face, lower eyelid retraction and superior globe displacement when there is maxillary bone hypertrophy at the orbital floor. Cherubism may have orbital manifestations including lower lid retraction, proptosis, diplopia, globe displacement and visual loss due to optic atrophy. Orbital involvement in cherubism may develop beyond puberty, after stabilization or regression of the lesions in the jaws.<sup>1-5</sup> We herein present computed tomography (CT) and three-dimensional (3D) CT imaging findings in two sporadic cases of che-

rubism with extensive, bilateral orbital involvement.

## CASE REPORTS

### PATIENT 1

A 12-year-old boy with known cherubism presented with facial deformity and bilateral exophthalmus. There was no associated trauma, tooth extraction, constitutional disturbance or pain. The parents and other relatives, as far as could be investigated, did not have any facial deformity. There was bilateral 6 mm proptosis with superior globe displacement and marked lower lid retraction. There was moderate restriction of upgaze in the left eye. In addition, there was scleral indentation due to maxillary bone hypertrophy at the orbital floor. The pupillary responses were normal and there was no optic atrophy, but visual field examination showed reduced sensitivity in the left eye. A panoramic radiograph of the mandible revealed multiloculated osteolysis involving the entire mandible with dislocated teeth. Only the mandibular condyles were not involved. X-ray of the remaining skeleton showed no abnormalities. CT scan showed soft tissue density masses occupying mandible, maxilla, and orbit with disrupted cortex (Figures 1A, B). 3D volume-rendered (VR) images were obtained from axial images in a separate workstation to display vascular and soft tissue structures. 3D-CT image exhibited a symmetrically

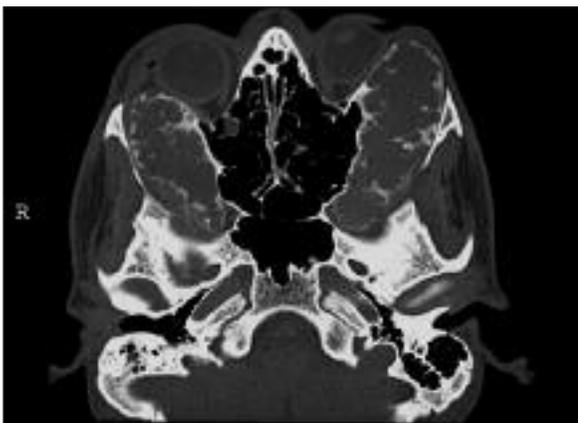
expanded mandible and maxilla. In addition, 3D CT scan confirmed bilateral bony masses protruding along inferior orbital walls towards orbital apices (Figures 2A, B).

### PATIENT 2

A 20-year-old male complained of slowly progressive superonasal globe displacement and bilateral inferior orbital masses of 5 years duration. He had a history of cherubism. His family history did not include any evidence suggestive of hereditary disease. The mandible and maxilla seemed expanded bilaterally, but no tenderness was noted.

On ophthalmology examination, there was slight restriction of upgaze in both eyes. His eyes were proptotic with superonasal globe displacement. Anterior segment examination was normal. Fundus examination after dilation of the pupils revealed healthy maculae and normal discs with no evidence of pallor.

Radiographs of the facial bones showed extensive involvement of the mandible and the maxilla (Figure 3). The normal trabecular architecture of both jaws was replaced with multilocular radiolucencies containing patchy foci of calcification. CT scans exhibited symmetrically expanded mandible and maxilla with extensive osteolysis and bone destruction of both edges of the maxilla. CT scans demonstrated multicystic bony lesions arising from



**FIGURE 1:** Case 1. In the bone window, axial (A) and coronal (B) CT images reveals bilateral inferolateral masses involving the orbital floors and producing marked superioromedial displacement of the orbital contents.



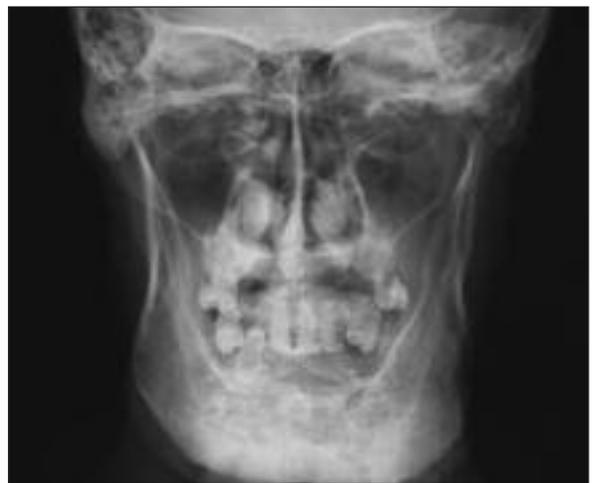
**FIGURE 2:** Case 1. (A) In the bone window, anterior view of three-dimensional volume-rendering CT scan shows gross bony hypertrophy of the orbital floors (L>R), (B) In the soft tissue window, three-dimensional volume rendering CT image shows expansile osseous remodelling of the jaws.

the orbital floors bilaterally (Figures 4 A, B). 3D CT scan of the face showed multilocular radiolucent areas with intervening solid tissues, involving the mandible and maxilla with marked extension of the lesion into the posterior of both orbits (Figure 5). The orbit had a reduced vertical dimension and the orbital contents were displaced superiorly. The lesion was very close to the right optic nerve but did not appear to infiltrate the orbital contents.

In both cases, laboratory tests, which included serum calcium, phosphorus, and alkaline phosphatase, were normal. No abnormality was found on clinical examination of the chest, abdomen, cardiovascular, or central nervous system. Laboratory tests, which included serum calcium, phosphorus, and alkaline phosphatase, were normal. There was no cortical break, fracture, or periosteal reaction within the affected bones. In both cases, because of the extensive maxillary involvement with extension into the orbital cavity, known expansile nature of the lesion and potential risk of compressive optic neuropathy, a multidisciplinary team performed surgery to debulk the orbital and maxillary lesions.

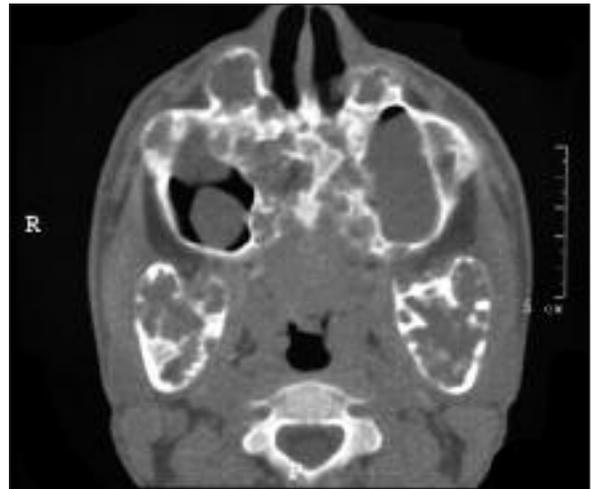
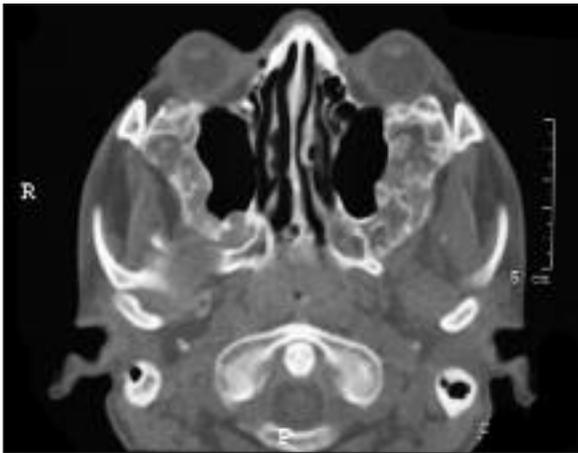
## DISCUSSION

Cherubism was first described by Jones in 1933 as familial multilocular cystic disease of the jaws. Cherubism is a rare benign condition with autosomal dominant inheritance. It appears to have 100% penetrance in male patients but only 50-70% pe-



**FIGURE 3:** Case 2. Plain X-ray of the jaw (anteroposterior view) shows involvement of the body and both ascending rami of the mandible with absence of the lower incisor teeth and displacement of other teeth. In addition, the radiograph shows expansile osseous remodelling of mandible.

netrance in female patients. A genome-wide search has established linkage to chromosome 4p16. The disease is not present at birth. The affected jaw begins to swell in early childhood and increases in size until puberty after which the disease does not progress further. In some cases the bone lesion regresses without any treatment. Approximately 175 cases of cherubism have been reported in the medical literature. The maxilla and mandible are usually bilaterally enlarged giving a fullness of the cheeks and jaw. Although the mandible is more frequently affected, lesions affecting the maxilla are



**FIGURE 4:** Case 2. (A, B) In the bone window, axial CT images through the mid-orbits and maxilla demonstrate maxillary involvement and decreased bilateral orbital volume.

more aggressive, as observed in our patients. This causes traction of the lower lids and with superior globe displacement.<sup>1, 3-8</sup>

A perivascular fibrosis resulting in reduced oxygenation of bone and an alteration of the mesenchyme during the development of bone have been considered in the pathogenesis of cherubism. Affected children are normal at birth with a mean age of presentation of seven years. The facial deformity consists of painless enlargement of the jaws up to the first decade and recede in adulthood.<sup>2, 4</sup>

Histologic examination of the lesions usually reveals numerous multinucleated giant cells. The collagenous stroma, which contains a large number of spindle-shaped fibroblasts, is considered unique because of its water-logged, granular nature. Numerous small vessels are present, and the capillaries exhibit large endothelial cells and perivascular capillary cuffing.<sup>1, 2, 8</sup>

Ramon and Engelberg proposed a grading system for cherubism based on involvement;<sup>4</sup>

*Grade 1:* involvement of both mandibular ascending rami,

*Grade 2:* grade 1 plus involvement of both maxillary tuberosities,

*Grade 3:* massive involvement of the whole maxillae and mandible except the condylar processes,



**FIGURE 5:** Case 2. Anterior view of three-dimensional volume rendering CT scan shows multicystic expansive bony lesions occupying the mandible and maxilla extension to the orbital floors bilaterally.

*Grade 4:* grade 3 plus involvement the floor of the orbits, causing orbital compression.

In our patients, the lesions were classified as grade 4, according to the grading system.

Cherubism may have orbital manifestations including lower lid retraction, proptosis, diplopia, globe displacement and visual loss due to optic atrophy.<sup>6</sup> However, orbital involvement secondary to cherubism has rarely been reported in the medical literature. In extensive literature search on orbital involvement secondary to cherubism, we found only two cases reports on this subject.<sup>5,6</sup>

Cherubism usually does not affect other parts of the skeleton or osseous metabolism; the bone markers phosphorous, serum calcium, and alkaline phosphatase are usually at normal levels with respect to age.<sup>4,6,10</sup> In our cases, a complete hematological workup was normal.

The typical radiographic appearance of cherubism is that of bilateral, well-defined, multilocular radiolucencies that can affect the mandible and the maxilla. Lesions often begin near the angle of the mandible and expand into the body and the ramus of the mandible. Preservation of mandibular condyles is regarded as the pathognomonic finding of cherubism. In both of our cases, mandibular condyles were preserved. Expanding lesions often cause thinning of the cortex and, in the maxilla, may cause obliteration of the maxillary sinus. In our cases, CT scanning helped to provide a clear delineation of the extent of disease, which was difficult on radiographs due to the overlap of the facial bones. On CT, we depicted bilateral osseous involvement, cortical thinning and expansile remodeling in the involved bones. In our cases, CT showed a multilocular appearance in the mandible created by the presence of bony septa and expansile remodeling and perforation in some regions. Moreover, we noticed the involvement of both maxillae. The lesion expanded into the maxillary sinus and caused the osseous involvement of orbital floors bilaterally. In addition, virtual reconstructions using 3D-CT imaging were also performed to provide a better anatomical visualization of the extent of the lesions. On the other hand, magnetic resonance imaging is only useful in determining the extent and localization of the lesions and the relation of the lesions with the orbit and the optic nerves.<sup>2,7-9</sup>

The differential diagnosis of cherubism includes giant cell granuloma of the mandible, odontogenic cyst, ameloblastoma, odontogenic fibroma, myxoma, hemorrhagic bone cyst, aneurysmal bone

cyst, craniofacial fibrous dysplasia (McCune Albright syndrome), familial gigantiform cementoma, brown tumor of hyperparathyroidism and Jaffe-Campanacci syndrome. Giant cell granuloma is usually unilateral and involves the patients between the ages of 20-40. Unlike cherubism, osteoclastoma rarely involves the mandible. Bilateral odontogenic cysts are not common in the first five years of life. Familial gigantiform cementoma is a rare osseous lesion characterized by cementum production in the lesions, and it usually involves the maxilla, not the mandible. Vascular tumors of facial bones usually follow trauma and usually are not confused with cherubism. Brown tumor and Jaffe-Campanacci syndrome are readily distinguished on the clinical grounds and are easily eliminated from the differential diagnosis. Particularly, cherubism should be distinguished from giant-cell reparative granuloma and McCune-Albright syndrome basically on clinical and radiological grounds and from hyperparathyroidism lesions on biochemical studies. Furthermore, hypertrophy of bilateral masseter muscles and pathologies related to the parotid gland should be kept in mind in the differential diagnosis of cherubism.<sup>1,4-14</sup>

The guidelines have not yet been established for the treatment of cherubism. Treatment must be individually determined for each patient, taking into account the extension of lesions, the potential for pathologic fracture, and the high probability of eventual regression.<sup>12</sup>

In conclusion, cherubism can lead to various types of ophthalmologic complications. Exophthalmus and loss of visual acuity due to compression of the optic nerve are the most common findings. Clinicians must be aware of these complications. We suggest that all cases of cherubism should be studied through CT and 3D-CT imaging because they can give much more information considering the extension and involvement of the facial bones, with a more specific spectrum of the lesion.

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